Efficacy and tolerability of Perampanel as only add-on in people with intellectual disability: data from the PEROC study

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BACKGROUND AND AIMS

Epilepsy affects 25% of individuals with intellectual disability (ID), with prevalence increasing alongside ID severity [1]. This population is characterized by higher rates of pharmacoresistance, polytherapy, and adverse effects (AEs) [2].

This study aimed to assess the efficacy and tolerability of perampanel (PER) as the only additional antiseizure medication (ASM) in patients with and without ID.

MATERIALS AND METHODS

We performed a subgroup analysis of patients included in the PEROC study [3], a retrospective, longitudinal, multicentre observational study including individuals with focal and generalized epilepsy receiving PER added to a single concomitant ASM. Retention, responders' rate, seizure-freedom, and AEs frequency were evaluated in patients with (ID+) and without (ID-) ID at 3, 6, and 12 months after PER introduction.

RESULTS

A total of 356 individuals (79 ID+ and 277 ID-) were included (table 1). A greater percentage of ID+ patients had a mild cognitive impairment. The median number of previous ASMs was 2 in ID- and 3 in ID+ patients. LEV was the most frequently used concomitant ASM in both groups. The PER median dose was 6 mg in both groups at 12 months (figure 1)

No significant difference in retention rates were observed at 3, 6, and 12 months between ID+ and ID- ($p>0.05$, figure 2a). Responder rates at 12 months were 73.3% in ID+ patients and 69.1%, in ID-, without significant difference ($p>0.05$). Seizure-free rates were lower in ID+ (37.%) than in ID- (46.3%), though the difference was not significant ($p>0.05$; figure 2b). The occurrence of AEs (mainly irritability, dizziness, and drowsiness) did not differ significantly between groups, occurring in 32.8% of ID+ and 24.5% of ID− patients, with PER withdrawal due to AES reported only in a small percentage of patients (table 2 and 3).

Characteristics (Patients: 356)	ID – (n: 277)	ID + (n: 79)
Age, years (median, IQR)	37 (22-54)	23 (17-37)
M/F, n (%)	109/168 (39/61)	38/41 (48/52)
Age at onset (median, IQR)	18 (10-40)	10 (2-15)
ID level		
mild	-	44 (55.7)
moderate	-	18 (22.8)
severe	-	17 (21.5)
Previous ASMs (median, IQR)	2 (1-3)	3 (2-4)
0–1, n (%)	127 (45.8)	15 (19)
≥2, n (%)	150 (54.2)	64 (81)
Concomitant ASM, n (%)		
LEV, n (%)	89 (32.1)	15 (19)
CBZ, n (%)	46 (16.6)	14 (17.7)
LTG, n (%)	35 (14.3)	10 (12.7)
VPA, n (%)	30 (10.8)	12 (15.2)

Table 1. Demographic and clinical characteristics of ID- and ID+ patients

Figure 1. Number of ID- and ID+ at each follow-up and concomitant PER median dose

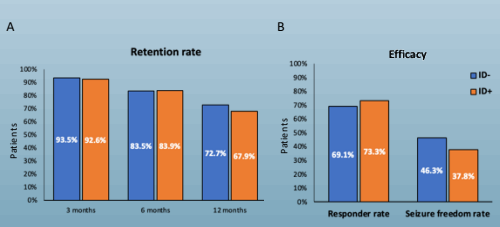

Figure 2. Retention (A) and responder and seizure freedom rate (B) in ID- and ID+

	ID-	ID+
Adverse events (AEs) (n, %)	66/269(24.5)	25/76 (32.8)
3 months	43/178 (24.2)	20/53 (37.7)
6 months	31/170 (18.2)	13/54 (24.1)
12 months	20/116 (17.2)	12/38 (31.6)
Serious AEs	9/269 (0.03)	1/60 (0.01)
PER discontinuation due to AEs	21/66 (7.8)	5/76 (6.7)

Table 2. Adverse events occurrence in ID- and ID+ patients.

Type (n, %)	ID-	ID+
Irritability	18 (6.7)	11 (14.5)
Dizziness	20 (7.4)	6 (7.9)
Drowsiness	8 (3)	5 (6.6)
Aggressiveness	6 (2.5)	1 (0.1)
Ataxia	6 (2.2)	1 (0.1)
Mood disorder	5 (1.8)	2 (0.3)

Table 3. Type of reported adverse events in ID- and ID+ patients.

DISCUSSION

Although the proportion of seizure-free patients was slightly lower in the ID cohort, responder and retention rates resulted comparable to those of ID− patients, thus demonstrating that PER, as single adjunctive therapy, is effective in individuals with ID. Interstingly, the incidence of AEs was similar between the two groups; while irritability was the most frequent AE in ID+ patients, it occurred in less than one-fifth of cases, supporting the favorable tolerability profile of PER in this vulnerable population.

CONCLUSION

PER, as single adjunctive therapy, is efficacious and well tolerated in individuals with ID., demonstrating efficacy and safety profiles comparable to those observed in patients without ID. Furthermore, PER may represent a valuable treatment option, making it a compelling choice for this unique patient population.

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